



Griscelli syndrome

Griscelli syndrome is an inherited condition characterized by unusually light (hypopigmented) skin and light silvery-gray hair starting in infancy. Researchers have identified three types of this disorder, which are distinguished by their genetic cause and pattern of signs and symptoms.

Griscelli syndrome type 1 involves severe problems with brain function in addition to the distinctive skin and hair coloring. Affected individuals typically have delayed development, intellectual disability, seizures, weak muscle tone (hypotonia), and eye and vision abnormalities. Another condition called Elejalde disease has many of the same signs and symptoms, and some researchers have proposed that Griscelli syndrome type 1 and Elejalde disease are actually the same disorder.

People with Griscelli syndrome type 2 have immune system abnormalities in addition to having hypopigmented skin and hair. Affected individuals are prone to recurrent infections. They also develop an immune condition called hemophagocytic lymphohistiocytosis (HLH), in which the immune system produces too many activated immune cells called T-lymphocytes and macrophages (histiocytes). Overactivity of these cells can damage organs and tissues throughout the body, causing life-threatening complications if the condition is untreated. People with Griscelli syndrome type 2 do not have the neurological abnormalities of type 1.

Unusually light skin and hair coloring are the only features of Griscelli syndrome type 3. People with this form of the disorder do not have neurological abnormalities or immune system problems.

Frequency

Griscelli syndrome is a rare condition; its prevalence is unknown. Type 2 appears to be the most common of the three known types.

Genetic Changes

The three types of Griscelli syndrome are caused by mutations in different genes: Type 1 results from mutations in the *MYO5A* gene, type 2 is caused by mutations in the *RAB27A* gene, and type 3 results from mutations in the *MLPH* gene.

The proteins produced from these genes are found in pigment-producing cells called melanocytes. Within these cells, the proteins work together to transport structures called melanosomes. These structures produce a pigment called melanin, which is the substance that gives skin, hair, and eyes their color (pigmentation). Melanosomes are formed near the center of melanocytes, but they must be transported to the outer

edge of these cells and then transferred into other types of cells to provide normal pigmentation.

Mutations in any of the three genes, *MYO5A*, *RAB27A*, or *MLPH*, impair the normal transport of melanosomes within melanocytes. As a result, these structures clump near the center of melanocytes, trapping melanin within these cells and preventing normal pigmentation of skin and hair. The clumps of pigment, which can be seen in hair shafts when viewed under a microscope, are a hallmark feature of the condition.

In addition to their roles in melanosome transport, the *MYO5A* and *RAB27A* genes have functions elsewhere in the body. Specifically, the protein produced from the *MYO5A* gene transports materials within nerve cells (neurons) that appear to be critical for cell function. The protein produced from the *RAB27A* gene is found in immune system cells, where it is involved in the release of certain compounds that kill foreign invaders (such as viruses and bacteria). Mutations in these genes impair these critical cell activities, leading to the neurological problems and immune system abnormalities found in Griscelli syndrome types 1 and 2, respectively.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- GS
- hypopigmentation immunodeficiency disease
- partial albinism with immunodeficiency

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Griscelli syndrome type 1
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1859194/>
- Genetic Testing Registry: Griscelli syndrome type 2
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1868679/>
- Genetic Testing Registry: Griscelli syndrome type 3
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1836573/>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Immune System and Disorders
<https://medlineplus.gov/immunesystemanddisorders.html>
- Health Topic: Skin Pigmentation Disorders
<https://medlineplus.gov/skinpigmentationdisorders.html>

Genetic and Rare Diseases Information Center

- Griscelli syndrome
<https://rarediseases.info.nih.gov/diseases/10913/griscelli-syndrome>

Educational Resources

- Centers for Disease Control and Prevention: Developmental Disabilities
<https://www.cdc.gov/ncbddd/developmentaldisabilities/>
- Disease InfoSearch: Griscelli Syndrome Type 1
<http://www.diseaseinfosearch.org/Griscelli+Syndrome+Type+1/3183>
- Disease InfoSearch: Griscelli Syndrome Type 2
<http://www.diseaseinfosearch.org/Griscelli+Syndrome+Type+2/3184>
- Disease InfoSearch: Griscelli Syndrome Type 3
<http://www.diseaseinfosearch.org/Griscelli+Syndrome+Type+3/3185>
- MalaCards: griscelli syndrome
http://www.malacards.org/card/griscelli_syndrome
- Orphanet: Griscelli disease
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=381

- The Merck Manual for Healthcare Professionals: Hemophagocytic Lymphohistiocytosis (HLH)
<http://www.merckmanuals.com/professional/hematology-and-oncology/histiocytic-syndromes/hemophagocytic-lymphohistiocytosis-hlh>
- University of Bristol: Melanin, Melanocytes, and Melanosomes
<http://palaeo.gly.bris.ac.uk/melanosomes/melanin.html>

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities
<http://aaid.org/>
- Immune Deficiency Foundation
<http://primaryimmune.org/>
- International Patient Organisation for Primary Immunodeficiencies
<http://www.ipopi.org/>
- Jeffrey Modell Foundation
<http://www.jmfworld.com/>
- The Arc: For People with Intellectual and Developmental Disabilities
<http://www.thearc.org/>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Griscelli+syndrome%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28griscelli+syndrome%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- ELEJALDE DISEASE
<http://omim.org/entry/256710>
- GRISCELLI SYNDROME, TYPE 1
<http://omim.org/entry/214450>
- GRISCELLI SYNDROME, TYPE 2
<http://omim.org/entry/607624>
- GRISCELLI SYNDROME, TYPE 3
<http://omim.org/entry/609227>

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